REMARKS

Applicants respectfully request entry of amendments to claims 20-22 and 24, and new claim 29. Claims 1-19 and 26-28 are withdrawn, without prejudice or disclaimer. Support for the amendments can be found throughout the specification, including paragraphs [0043], [0045], [0047], [0051], [0057]-[0061], [0089], [0094], Examples 8 and 10-12, and the originally filed claims and, therefore, do not add new matter.

Applicants submit that pending claims 20-25 and 29 are in condition for allowance, and respectfully request that the claims as amended be entered.

Objections

Applicants have corrected the dependency for the claims.

For this reason, Applicants respectfully request that the objection be withdrawn.

Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 20-25 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

Applicants traverse the rejection as it might apply to the new and amended claims for the reasons given below.

Claims 20-22 are no longer dependent on non-elected claim 1, and no longer recite the phrase identified, so the rejection is rendered moot. Applicants have amended the claims to recite "deposited as ATCC accession No. CRL-12461 or cells clonally derived from cells deposited as ATCC accession No. CRL-12461." The term "ATCC accession NO." is a term of art and would be known to one of skill in the art generally as an identifier of a particular cell type. As such, one of skill in the art would understand the metes and bounds of the term.

Regarding claim 22, and the phrase "blood borne molecules," the claim has been amended to recite "blood borne toxic solutes" (see, e.g., paragraph [0057] of the instant specification). Since the removal of toxic solutes is an intrinsic property of the liver, one of skill in the art would know the metes and bounds of the term. Further, regarding the phrase "release of molecules," the claim has been amended to recite "release of protein and low molecular

weight products" (see, e.g., paragraph [0043] of the instant specification). Since "liver specific activity" is expressly recited in the specification to include synthesis and secretion of protein and low molecular weight products, one of skill in the art would know the metes and bounds of the term.

Regarding claim 21, while Applicants do not acquiesce to the reasoning offered in the Action, and to expedite prosecution towards allowance, the claim has been amended to clarify the positive process steps.

For these reasons, Applicants respectfully request that the rejections be withdrawn.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 20-25 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement.

Applicants traverse the rejection for the reasons given below.

The Office Action alleges, in pertinent part, that the claims embrace any cell line derived from the parent C3A cell line. Further, the Action intimates that the specification does not provide sufficient guidance to practice the full scope of the invention, citing Strain et al. as a reference to demonstrate the limitations of the use of bio-artificial livers, suggesting that issues related to crucial liver function, polarization of aggregates, failure to describe the kind of device to be used, potential tumor formation, type of disease that can be treated using a device, and clinical difficulties, could not be appreciated using the instant specification as a guide. Applicants respectfully submit that such allegations are incorrect.

Notwithstanding the amendments to the claims, the position regarding clinical data and tumor formation is not within the purview of the United States Patent and Trademark Office. As stated in Scott v. Fenny, 32 U.S.PQ.2d 1115, 1120 (Fed. Cir. 1994), "[t]esting for the full safety and effectiveness of a prosthetic device is more properly left to the Food and Drug Administration (FDA)." Scott v. Finney goes on to say,

> "Title 35 does not demand that such human testing occur within the confines of Patent and Trademark Office (PTO) proceedings. Cf. In re Sichert, 566 F.2d 1154, 1160, 196 U.S.P.Q. 209, 214 (CCPA 1977) (rejecting lack of safety

> challenge to utility of claimed drug); In re Anthony, 414 F.2d 1383, 1395, 162 U.S.P.Q. 594, 604 (CCPA 1969)("Congress has given the responsibility to the FDA, not to the [PTO], to determine . . . whether drugs are sufficiently safe . . . .") (citation omitted); In re Watson, 517 F.2d 465, 476, 186 U.S.P.Q. 11, 19 (CCPA 1975)."

Thus, the position taken by the Action, i.e., to meet standards normally associated with the FDA approval, is not appropriate.

Nevertheless, the specification clearly teaches 1) critical liver functions that must be considered (see, e.g., paragraph [0044]), 2) use of polarized aggregates in hollow cartridge devices (see, e.g., paragraph [0060]), including the devices themselves (see, e.g., paragraphs [0057]-[0060]), 3) cell density to achieve necessary function (see, e.g., paragraph [0060]), including the use of C3A hepatocytes with fibroblasts (see, e.g., paragraph [0062]), and 4) a specific disease to be treated (e.g., Fulminant hepatic failure (FHF), at paragraphs [0054] and [0055]), including that it is well known that subjects suffering from FHF have low albumin (see, e.g., http//homepage.mac.com/guitarbloke/Surgical_sieve/Hepatobiliary/Liver/Hepat_FHF.html), a specific protein that is produced by the cells as claimed (see, e.g., Example 4, Table 1).

Further, because the claims expressly recite a specific C3A cell type to be used in the device/methods, the claims do not embrace "any and all" C3A derivatives. Moreover, the claims are enabled because the specification provides prediction of function based on tested and workable materials and designs of prosthetics which were well known in the art at the time the application was filed (see, e.g., paragraphs [0058]-[0059]).

Thus, one of skill in the art could practice the invention as claimed, in the absence of undue experimentation. For these reasons, Applicants respectfully request that the rejection, including as it may be applied to the new and amended claims, be withdrawn.

Rejection Under 35 U.S.C. §103

Claims 20 and 21 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Spiering et al., in view of Price et al.

Applicants traverse the rejection as it might apply to the new and amended claims, including claims dependent therefrom, for the reasons given below.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First there must be some suggestion or motivation in the references themselves or in knowledge generally available to one of skill in the art, to modify the reference or combine the reference teachings. Second, there must be a reasonable expectation of success. And, finally the prior art reference (or references when combined) must teach all claim limitations. The teaching or suggestion and reasonable expectation of success must both be found in the prior art and not in Applicants' disclosure. (See MPEP §706.02(j)).

Applicants submit that because the cited references do not teach all the claim limitations, one of skill in the art would not be motivated to combine the reference teachings.

The Office Action alleges, in pertinent part, that Spiering et al. is silent with respect to teaching growing C3A cells in serum free medium. The Action then provides Price et al. to cure the deficiency identified in the primary reference. However, review of Spiering et al. demonstrates that the reference does not teach cells deposited as ATCC accession No. CRL-12461 or cells clonally derived from cells deposited as ATCC accession No. CRL-12461, elements presently recited in the claims.

Applicants submit that, in fact, the cited reference "teaches away" from the present invention. This is so, because the output of albumin/day/cell as recited in Spiering et al. (i.e., 2×10^{-9} g of human albumin/day/cell) would be lower than the intrinsic output of albumin observed for the cells as claimed (i.e., 2.2×10^{-8} g of human albumin/day/cell, see Table 2). Therefore, one of skill in the art would only extract from such a teaching that the cells of Spiering et al. would not have the properties of the cells as claimed. This is not cured by Price et al. As such, the references when combined do not teach cells having an equivalent albumin output as those cells recited in the claims. Therefore, the reference teaches away, since the impression left to the

skilled artisan is that the device/method would not have the property sought by Applicants. In re Caldwell, 319 F.2d 254, 256, 138 U.S.P.Q. 243, 245 (CCPA 1963).

Because the teachings of Spiering et al. would not result in cells as recited when combined with the teachings of Price et al., one of skill in the art would not have an expectation of success since the invention as claimed would not be achieved in view of such teachings. Therefore, one of skill in the art would not be motivated to combine such teachings.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed, there is no motivation to combine the cited references, thus, no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the rejection, including as it might be applied against the new and amended claims, be withdrawn.

Conclusion

Applicants submit that pending claims 20-25 and 29 are in condition for allowance. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this submission.

No fee is deemed necessary with the filing of this paper. However, the Commissioner is hereby authorized to charge any fees required by this submission, or credit any overpayments, to Deposit Account No. 07-1896 referencing the above-identified docket number. A duplicate copy the Transmittal Sheet is enclosed.

Respectfully submitted,

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